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THE INFLUENCE OF A COOKED MEAT MEAL ON CREATININE PLASMA CONCENTRATION AND CREATININE CLEARANCE

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1 The influence of a meal containing cooked meat (225 g) on creatinine plasma concentration, creatinine urinary excretion and creatinine clearance was determined in six healthy male subjects.

2 The meat meal produced an average 52% increase in creatinine plasma concentration within 1.5 to 3.5 h after ingestion. The 24 h area under the creatinine plasma concentration-time curve increased by about 19%. Urinary creatinine excretion during 24 h increased by an average of 13%. Creatinine clearance was not altered in response to the meal of cooked meat.

Introduction

Serum creatinine concentration is the most frequently used clinical estimate of renal function, although creatinine clearance is the more appropriate and direct index. The relationship between serum creatinine and creatinine clearance is affected by age, sex, and weight or body build (Kampmann & Molholm Hansen, 1981). Recently, several investigators have shown an increase in serum creatinine concentration in man (Jacobsen *et al.*, 1979, 1980) and dogs (Watson *et al.*, 1981) after ingestion of a meal high in cooked meat protein. This change may be associated with absorption of creatinine present in cooked meat. It has been suggested that creatinine clearance remains unchanged (Jacobsen *et al.*, 1980) or increases (Sherman, 1981) in response to such a meal. The purpose of this study was to examine the temporal pattern of serum creatinine concentration and creatinine clearance under conditions which were controlled carefully for nutritional factors.

Methods

Protocol

Six healthy adult male subjects participated in the study (average age and range: 31, 26–38 years; average weight and range: 73, 65–82 kg). The study was conducted during two consecutive days. On day one each subject ate a control breakfast devoid of meat. Three subjects ingested a meal high in non-meat protein (62 g; subjects 1, 4, and 5) and three subjects ate a meal low in non-meat protein (11.5 g). All subjects ingested limited amounts of non-meat protein for lunch (16.7 g) and dinner (20.8 g). Subjects eating the high protein breakfast on day one consumed a total of 2190 calories on that day, whereas the subjects eating the low protein breakfast consumed a total of 1918 calories. Sodium content was nearly identical for both diets.

On the second (experimental) day each subject ate a breakfast containing 225 g of boiled beef. The beef (450 g) was boiled for 1.5 h and yielded 225 g after cooking. Lunch and dinner were the same as on day one. The total number of calories (1949) and sodium intake were comparable to those on day one. Fluids were allowed *ad libitum* on both days.

An indwelling venous catheter containing heparin was placed into a forearm vein prior to breakfast on day one and all but the last sample on day two were obtained through the catheter. Approximately 1 ml of blood was withdrawn and discarded prior to obtaining a blood sample. Fresh heparin (0.5 ml, 100 units/ml) was instilled after blood sampling. Frequent blood samples and exactly timed urine collections were obtained during both study days. Blood samples were taken at times to correspond to the midpoint of the urine collection intervals.

Analytical methods

Plasma and urine creatinine concentrations were

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determined by a high pressure liquid chromatographic procedure which is specific and sensitive for creatinine (unpublished). Briefly, the method involves filtration of plasma and injection (20 μl) of the filtrate or diluted urine into the chromatograph using an ultrasphere ODS (5 μ) column and a Co:Pell ODS guard column. The mobile phase consisted of a mixture of 0.05 M sodium acetate (pH 6.5) and acetonitrile (98/2, by volume) at a flow rate of 1 ml/min. Detection was achieved at 254 nm. Under these conditions creatinine had a retention time of 2.6 min. Creatinine concentrations were determined from calibration curves in plasma or urine which were prepared daily. All samples were assayed within 1 week of collection.

Data analysis

The amount of creatinine excreted during sequential collection periods was determined from the product of urine creatinine concentration and urine volume. Creatinine excretion rate was calculated by dividing the amount excreted by the time interval of collection. Creatinine clearance was determined by dividing excretion rate by creatinine plasma concentration at the midpoint of the collection interval. Since frequent plasma and urine samples were obtained, several values of creatinine clearance and estimates of variance could be calculated during each day (5–9 values per subject per day). A one point calculation of creatinine clearance was also made based upon the ratio of the 24 h cumulative urinary creatinine excretion to the area under the 24 h creatinine plasma concentration-time curve. The area was determined by the trapezoidal rule. Statistical comparison of results (control *vs* experiment) was achieved by use of the paired Student's *t*-test.

Results

Figure 1 illustrates creatinine plasma concentrations as a function of time after the control and experimental (cooked meat) breakfasts. Creatinine concentrations remain quite stable during the control day with percentage coefficients of variation ranging from 2.2 to 4.3%. The low and high protein non-meat control meals produced comparable creatinine plasma concentrations suggesting that these meals do not provide a source of exogenous creatinine. In contrast, and for each subject, there is a dramatic rise in concentration during the experimental day following the breakfast of cooked meat. The percentage increase in creatinine concentration relative to the mean value during the control day averaged 52% and ranged from 36 to 65%. The maximum concentration was achieved at an average of 2 h after the meal (range, 1.5 to 3.5 h).

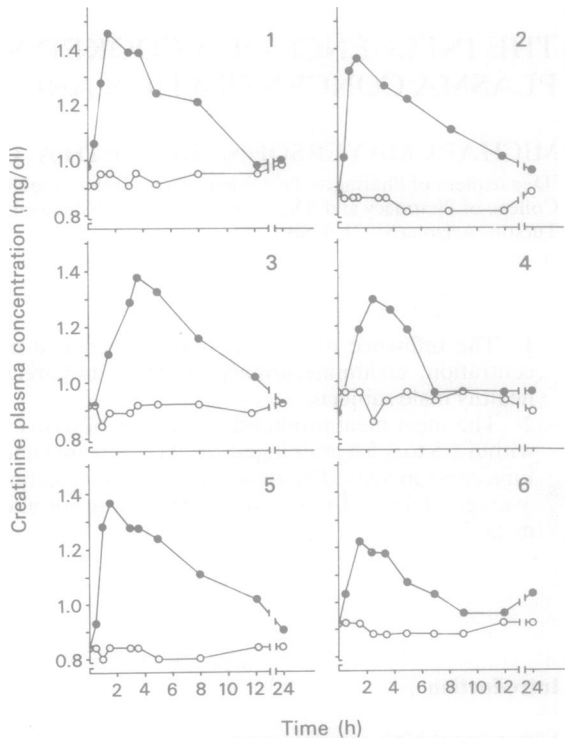

Figure 1 Creatinine plasma concentration as a function of time following a control breakfast devoid of meat protein (○) and following an experimental breakfast of cooked meat protein (●). 1 mg creatinine/100 ml ≡ 88.4 μmol/l.

The influence of the experimental meal on the other measured parameters is summarized in Table 1. There is a significant increase in the 24 h area under the creatinine plasma concentration-time curve and in the 24 h urinary creatinine excretion. The relative increase in these two parameters is approximately the same as may be seen by reference to the ratio of the experimental to the control values (E/C). There is an average 19% increase in area and a 13% increase in the amount of creatinine excreted.

Creatinine clearance has been calculated from a one point determination (based upon total 24 h area and urinary excretion) and from the mean of multiple determinations during both study days. Those values are presented in Table 1. With the exception of subject 1 and subject 3 (experimental day) the values for creatinine clearance within each subject are quite consistent with percentage coefficients of variation ranging from 7 to 14% among the subjects. Because of the approximate proportional change in area and urinary excretion after the meat meal, creatinine clearance remains unchanged compared to the control day.

Table 1 Changes in creatinine plasma concentration, urinary excretion and creatinine clearance after a control (C) and an experimental (E) cooked meat meal

Subject	AUC[a] (mg ml^{-1} h) C	E	Ratio E/C	Urinary creatinine[b] (g) C	E	Ratio E/C	Creatinine clearance[c] (ml/min) C	E	Ratio E/C	Creatinine clearance[d] (ml/min) C	E	Ratio E/C
1	0.224	0.265	1.18	1.83	2.18	1.19	136	137	1.01	138 ± 32	134 ± 34	0.97
2	0.222	0.257	1.16	2.03	2.15	1.06	153	140	0.92	158 ± 14	140 ± 13	0.89
3	0.199	0.254	1.28	1.84	‖	‖	154	‖	‖	188 ± 20	166 ± 51	0.88
4	0.199	0.257	1.29	1.66	1.94	1.17	139	126	0.91	143 ± 11	130 ± 14	0.91
5	0.220	0.240	1.09	1.40	1.53	1.09	106	106	1.00	103 ± 8	110 ± 14	1.07
6	0.215	0.242	1.13	1.28	1.44	1.13	99	99	1.00	105 ± 7	110 ± 15	1.05
Mean	0.213	0.253	1.19	1.67	1.85	1.13	132	122	0.97	139	132	0.96
± s.d.	0.011	0.010	0.08	0.29	0.35	0.05	23	18	0.05	32	21	0.08
Significance		$P < 0.005$			$P < 0.02$			NS			NS	

[a] AUC = Area under the creatinine plasma concentration-time curve (0–24 h); [b] = Amount of creatinine excreted in urine (0–24 h); [c] Determined from the ratio of the 24 h urinary creatinine to the 24 h AUC; [d] Mean ± s.d. of creatinine clearance determined from creatinine excretion rate and midpoint creatinine plasma concentration: ‖ Incomplete urine collection: Paired Student's *t*-test; NS = not significantly different ($P > 0.05$).

Similarly, from the multiple determinations, creatinine excretion rate increases proportionately with creatinine plasma concentration resulting in no change in creatinine clearance between study days. Neither method of clearance calculation indicates a significant change in clearance in response to the cooked meat meal. The average ratio of creatinine clearance (E/C) from the one point calculation, 0.97 (range, 0.91–1.01) is identical to the average obtained from the multiple determinations, 0.96 (range, 0.88–1.07).

Discussion

The influence of the ingestion of cooked meat protein on creatinine plasma concentrations has been recognized or alluded to for some time (Camara *et al.*, 1951; Sargent & Johnson, 1956; Rapoport & Husdan, 1968; Pasternak & Kuhlback, 1971). As noted above, creatinine plasma concentrations increased an average of 52% after the cooked meat meal, compared to control values. Jacobsen *et al.* (1979, 1980) reported a 100% increase in serum creatinine concentration. The smaller relative increase found here may be as a result of a smaller meat meal (225 g *vs* 250–300 g) and/or because a more specific analytical procedure was employed. In addition to the assay employed here, plasma samples from two subjects were also analysed by two clinical laboratories which use an automated colorimetric assay. Creatinine concentrations were greater by the latter method compared to the chromatographic method used in this study (unpublished).

The cooked meat meal resulted in an average of 180 mg urinary creatinine in excess of that excreted during the control day. Presumably this arises from absorption of exogenous creatinine present in the cooked meat. Camara *et al.* (1951) have determined a creatinine content of about 1.5 mg/g boiled beef. Based upon that value the meal employed in this study would contain about 340 mg creatinine. However, the actual amount of creatinine absorbed will depend upon absorption efficiency, type of meat and the duration of cooking.

Although there is a marked increase in creatinine plasma concentration after the meat meal there is no change in creatinine clearance. This is a result of the fact that urinary creatinine excretion increases in proportion to the change in plasma concentration. In fact one would not anticipate seeing a change in creatinine clearance since there is no reason to expect an alteration in renal function in response to creatinine absorption. Jacobsen *et al.* (1980) also indicate no change in creatinine clearance after a cooked meat meal, although they have not reported their data.

It must be recognized that a rigorous protocol was

employed in this study in order to determine unequivocally the influence of a cooked meat meal on creatinine clearance. Such an approach is obviously not realistic in a clinical setting, although our findings are pertinent to that setting. Two problems may arise during the routine estimation of renal function with reference to creatinine. If a day-time blood sample is obtained within several hours following a meal containing cooked meat, a spuriously high creatinine serum concentration will be reported. This is indicated from the results in Figure 1. Alternatively, if a cooked meat meal is ingested during a 24 h urine collection a spuriously high value will be obtained for creatinine excretion. If that value is related to a fasting creatinine serum concentration an overestimate of creatinine clearance will be made, as has been reported by one investigator (Sherman, 1981). The most practical precaution to avoid both of the above potential problems is to caution patients to eat meals devoid of cooked meat shortly before and during determinations of serum or urinary creatinine concentrations.

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